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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/431,594	11/01/1999	JEFFERY J. WHEELER	16303-002430	8936

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WILLIAM B KEZER
TOWNSEND AND TOWNSEND AND CREW LLP
TWO EMBARCADERO CENTER
8TH FLOOR
SAN FRANCISCO, CA 941113834

EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/431,594	WHEELER ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42 and 44-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42 and 44-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11-1-99*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 5-17-04.

Claims 42, 44-75 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claims 42, 44-61, 63-75 are rejected under 35 U.S.C. 102(e) as being anticipated by Choi et al for the same reasons of record set forth in the Office actions mailed 8-9-01, 5-16-02, 3-25-03 and 12-15-03.

Applicant's arguments filed 5-17-04 have been fully considered but they are not persuasive. Applicants argue that Choi does not teach that the encapsulation methods disclosed in their specification (e.g. the method of example 9) are to be used for nucleic acids. Contrary to Applicants' assertions, and as mentioned previously in the Office actions mailed 8-9-01, 5-16-02 and 3-25-03 in addressing Applicants' arguments to this rejection, the instant claims are not drawn to methods, but are drawn to compositions. In addition, Choi, at claims 1, 4, 5, 16 and 17, disclose compositions comprising liposomal formulations that include "gene constructs" and "oligonucleotides" for

therapeutic use, which liposomal compositions are explicitly used "for delivering bioactive agents to cells comprising encapsulating the agent in a liposome" (*e.g. see claims 6 and 27). The intention of Choi is clear - to provide liposomal formulations for encapsulating bioactive agents, thereby increasing the circulating half-life of these delivery constructs in vivo (see e.g. columns 20-22, examples 7-10, delineating compositions and methods for entrapping bioactive agents and thereby increasing circulating time of the agents in serum. The entire focus of Choi addresses compositions and methods for encapsulating bioactive agents for increasing target cell delivery in an animal. Absent evidence to the contrary, the prior art compositions meet the structural limitations of the claimed compositions and are therefore presumed to have the same functional properties as Applicants' claimed compositions. Furthermore, Applicants' have not provided any unexpected results that would indicate that the particles synthesized in the instant disclosure are distinct from the liposomal compositions previously disclosed by Choi.

Applicants argue that Choi teaches formation of nucleic acid-lipid complexes that are exactly as those disclosed in the prior art (e.g. by Wang et al and Hyde et al, see Applicants' arguments on pages 10-11, filed 5-17-04), and these (previously disclosed) compositions for nucleic acids are meant to be distinct from the other, encapsulating compositions that Choi discloses for inclusion of all other bioactive agents. Applicants are correct that Choi reviews previously existing liposomal formulations traditionally used to deliver nucleic acids. This is clearly stated in column 18: "The efficiency of this transfection has often been less than desired, for various reasons. One is the tendency

for cationic lipids complexed to nucleic acids to form unsatisfactory carriers. These carriers are improved by the inclusion of PEG lipids." It is unclear how Applicants interpret this section of Choi to distinguish encapsulating nucleic acids from all other bioactive compounds taught by Choi. Applicants' interpretation of Choi regarding the specific exclusion of nucleic acid compositions from all other encapsulated bioactive compounds is misplaced. After reviewing the existing liposomal compositions traditionally used for nucleic acid, and their shortcomings, Choi explicitly state: "The invention will be better understood by reference to the following examples, which are intended to illustrate aspects of the invention..." (col.18, lines 24-26), after which follows the encapsulation compositions and methods for increasing the circulation time/plasma stability of bioactive agents (e.g. examples 1-10). Contrary to Applicants' assertions, there is nothing in Choi to make this subjective interpretation to exclude nucleic acids from the encapsulating compositions taught previously by Choi. Absent concrete evidence to the contrary, the liposomal formulations prepared by Choi undoubtedly qualify as prior art for encapsulating nucleic acids. There is no evidence that the compositions and methods disclosed by Choi could not be used to entrap nucleic acid molecules. They are the same compositions as taught in the instant application, and hence anticipate the claimed invention.

Applicants argue that example 11, and not the remaining parts of the Choi patent, refers to nucleic acid compositions because this section teaches that the incorporation of PEG-lipids into cationic liposomes prevents their aggregation (see last paragraph of Applicants' arguments, page 11). It is unclear how the prevention of

aggregation of liposomes by the incorporation of PEG-lipids leads to the conclusion that Choi teaches encapsulation of all bioactive agents disclosed in this patent other than nucleic acids.

Applicants also argue that the declaration of Semple makes clear that the liposomal formulations of Choi are meant to exclude nucleic acids, and that the pending claims of the instant application provide novel methods by which nucleic acids are encapsulated within cationic liposomes that include a conjugated lipid such as the PEG-lipid, preventing aggregation of liposomal particles. It is unclear why Applicants' representative repeatedly states that the instant claims include methods. The instant claims are drawn to compositions, not methods. Limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed.Cir. 1993). The compositions of the instant invention have identical chemical compositions to those disclosed by Choi and therefore cannot have mutually exclusive properties. (See *In re Spada*, 911 F2d 705, 709, 15 USPQ2d1655, 1658 (Fed. Cir. 1990).

Applicants argue further that a comparison of the methods that Choi cites in the prior art, in reviewing previously existing liposomal compositions utilized for nucleic acid delivery, clearly indicates the differences between the instantly claimed compositions and those of Choi. Contrary to Applicants' assertions, the citations by Choi of prior compositions utilized for nucleic acid delivery were to contrast the liposomal compositions disclosed and claimed by Choi, not to limit the patent to previously described compositions. Applicants misconstrue Choi, and their reiteration of previously

known liposomal formulas (e.g. of Monck et al, Mauer et al) do not limit Choi's disclosure of the instantly claimed compositions, including encapsulated nucleic acid compositions. Applicants argue that Choi do not teach nucleic acid lipid particles of the instant invention because they don't teach encapsulation in the lipid and resistance in aqueous solution to degradation with a nuclease. Contrary to Applicants' assertions, the compositions disclosed by Choi are identical to those taught in the instant application and since the structural limitations of the claimed compositions are met by the prior art compositions, the prior art compositions are presumed to have the same functional properties (see MPEP 2112.02).

Claims 42, 44-61, 63-64, 67-75 are rejected under 35 U.S.C. 102(e) as being anticipated by Holland et al for the same reasons of record set forth in the Office action mailed 12-5-03.

Applicant's arguments filed 5-17-04 have been fully considered but they are not persuasive. Applicants argue that, as with Choi, Holland discloses the same methods as Choi for preparing classical liposomes and do not teach the nucleic acid lipid particles of the present invention. Contrary to Applicants' assertions, Holland discloses the same compositions as those claimed in the instant application. The instant claims are drawn to products, not to methods for the synthesis of the claimed product. And as such, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPZ2d 1057 (Fed. Cir. 1993). Applicants have not provided any evidence that the compositions disclosed by Holland do not necessarily possess the characteristics of the claimed compositions. When the prior art teaches the identical

chemical formulations as those taught in the instant application, the properties that Applicant discloses (i.e. encapsulation of nucleic acids and resistance from nuclease degradation) are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Choi et al for the same reasons of record set forth in the Office action mailed 12-15-03.

Applicant's arguments filed 5-17-04 have been fully considered but they are not persuasive. Applicants argue that because Choi does not teach nucleic acid lipid particles that comprise encapsulated nucleic acids that are resistant to nuclease degradation, the 103 rejection is improper. Contrary to Applicants' assertions, Choi teaches the nucleic acid lipid compositions of the instantly claimed invention, and so these identical chemical formulations impart the properties that Applicant discloses (See the above discussions addressing the 102 rejections of record). The bioactive agents in these compositions anticipated by Choi include oligonucleotides intended to block production of a protein with a target cell (see col. 17, line 66-col. 18, line 24 of Choi. See also claims 4, 5, 16 and 17 of Choi). The genus of nucleic acids used to block protein expression includes ribozymes, and was well known in the art at the time the instant invention was made. Therefore the obviousness rejection of record is proper.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ
9-27-04